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=> d stat que l28

L21           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "THROMBOSPONDIN 2 (CATTLE
                CLONE P268C1 PRECURSOR)"/CN
L22           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "THROMBOSPONDIN-2 (HUMAN
                CLONE PSECTAG)"/CN
L23             SEL  PLU=ON  L21 1- CHEM :        3 TERMS
L24             SEL  PLU=ON  L22 1- CHEM :        3 TERMS
L25           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L23
L26           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L24
L27          88 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L25 OR L26 OR (THROMBOSPONDIN?
                 OR TSP)(W)2
L28          35 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L27 AND (?CANCER? OR ?CARCINOM
                ? OR ?TUMOR? OR ?NEOPLAS? OR ?MALIG? OR SKIN OR ?DERM?)


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=> d ibib abs hitrn l28 1-35


L28  ANSWER 1 OF 35  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         2001:526224  HCAPLUS
TITLE:                    Gene expression profile for detecting and
                          characterizing a neoplasm
INVENTOR(S):              Sager, Ruth; Martin, Katherine J.; Pardee, Arthur
PATENT ASSIGNEE(S):       Dana-Farber Cancer Institute, Inc., USA
SOURCE:                   PCT Int. Appl., 64 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
```

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001051664	A2	20010719	WO 2001-US101081	20010112

W: CA, JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

PRIORITY APPLN. INFO.: US 2000-175669 P 20000112

AB Disclosed are methods of detecting **neoplasms**, such as breast **carcinomas**, using differentially expressed genes. The genes differentially expressed in **cancerous** and non-**cancerous** breast cells as well as blood cells from breast **cancer** patients and normal controls were compared using differential display anal. and hybridization array anal. The invention provides a method of diagnosing a **neoplasm**, assessing the prognosis of a subject with **neoplasm** and the efficacy of **antitumor** agents. The genes related to **neoplasm** are grouped into six clusters: estrogen receptor (ER) status-assocd. cluster I; ER status-assocd. cluster II; clin. stage-assocd. cluster; **tumor** size-assocd. cluster; disseminated **tumor** assocd. cluster I; and disseminated **tumor** independent genes. Also disclosed are methods of identifying agents for treating **neoplasms**.

IT INDEXING IN PROGRESS

L28 ANSWER 2 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:455823 HCAPLUS
TITLE: **Thrombospondin-2** plays a protective role in multistep carcinogenesis: a novel host anti-**tumor** defense mechanism
AUTHOR(S): Hawighorst, Thomas; Velasco, Paula; Streit, Michael; Hong, Young-Kwon; Kyriakides, Themis R.; Brown, Lawrence F.; Bornstein, Paul; Detmar, Michael
CORPORATE SOURCE: Cutaneous Biology Research Center and Department of Dermatology, Massachusetts General Hospital and Harvard Medical School, Charlestown, MA, 02129, USA
SOURCE: EMBO J. (2001), 20(11), 2631-2640
CODEN: EMJODG; ISSN: 0261-4189
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The angiogenic switch during **tumorigenesis** is thought to be induced by a change in the balance of pro-angiogenic and anti-angiogenic factors. To elucidate the biol. role of the endogenous angiogenesis inhibitor **thrombospondin-2** (**TSP-2**) during multistep carcinogenesis, we subjected **TSP-2** -deficient and wildtype mice to a chem. **skin** carcinogenesis regimen. Surprisingly, **TSP-2** expression was strongly upregulated in the mesenchymal stroma of wild-type mice throughout the consecutive stages of **tumorigenesis** whereas the angiogenesis factor, vascular endothelial growth factor, was induced predominantly in **tumor** cells. **TSP-2** deficiency dramatically enhanced susceptibility to **skin** carcinogenesis and resulted in accelerated and increased **tumor** formation. The angiogenic switch occurred in early stages of pre-**malignant tumor** formation, and **tumor** angiogenesis was significantly enhanced in **TSP-2**-deficient mice. While **TSP-2** deficiency did not affect **tumor** differentiation or proliferation, **tumor** cell apoptosis was significantly reduced. These results reveal upregulation of an endogenous angiogenesis inhibitor during multistep **tumorigenesis** and identify enhanced stromal **TSP-2** expression as a novel host anti-**tumor** defense mechanism.

REFERENCE COUNT: 54
REFERENCE(S): (1) Bein, K; J Biol Chem 2000, V275, P32167 HCAPLUS

(2) Bergers, G; Nature Cell Biol 2000, V2, P737 HCAPLUS
(3) Bergers, G; Science 1999, V284, P808 HCAPLUS
(4) Bolontrade, M; Carcinogenesis 1998, V19, P2107 HCAPLUS
(5) Bornstein, P; Matrix Biol 2000, V19, P557 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 3 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:338762 HCAPLUS
DOCUMENT NUMBER: 134:362292
TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
INVENTOR(S): Farr, Spencer
PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-165398 P 19991105
US 2000-196571 P 20000411

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to det. the hypersensitivity of individuals to a given agent, such as drug or other chem., in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes assocd. with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes assocd. with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes assocd. with hypersensitivity. The expression of the genes predetd. to be assocd. with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and app. useful for identifying hypersensitivity in a subject are also disclosed.

L28 ANSWER 4 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:216353 HCAPLUS
DOCUMENT NUMBER: 134:308545
TITLE: Extracellular matrix metalloproteinase 2 levels are regulated by the low density lipoprotein-related scavenger receptor and **thrombospondin**

AUTHOR(S): Yang, Zhantao; Strickland, Dudley K.; Bornstein, Paul
CORPORATE SOURCE: Department of Biochemistry, The University of Washington, Seattle, WA, 98195, USA

SOURCE: J. Biol. Chem. (2001), 276(11), 8403-8408
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have recently shown that the adhesive defect obsd. in **dermal** fibroblasts derived from **thrombospondin 2** (TSP2)-null mice results from an increase in matrix metalloproteinase 2 (MMP2) levels. Adhesion was restored by replacement of TSP2 and by inhibitors of MMP2 activity. In pursuing the observation that TSP2 and MMP2 interact, we now demonstrate that this interaction is required for optimal clearance of extracellular MMP2 by fibroblasts. Since TSP2 is known to be endocytosed by the scavenger receptor, low d. lipoprotein receptor-related protein (LRP), we detd. whether interference with LRP function affected fibroblast adhesion and/or extracellular MMP2 levels. Addn. of heparin, which competes for the binding of TSP2 to LRP coreceptor proteoglycans, inhibited adhesion of control but not TSP2-null cells, and a blocking antibody to LRP as well as the LRP inhibitor, receptor-assocd. protein, also inhibited adhesion and increased MMP2 levels only in control fibroblasts. TSP2 did not inhibit active MMP2 directly and did not inhibit the activation of pro-MMP2. Finally, the internalization of 125I-MMP2 was reduced in TSP2-null compared with control fibroblasts. We propose that clearance of MMP2-TSP2 complexes by LRP is an important mechanism for the regulation of extracellular MMP2 levels in fibroblasts, and perhaps in other cells. Thus, some features of the phenotype of TSP2-null mice, such as abnormal collagen fibrillogenesis, accelerated wound healing, and increased angiogenesis, could result in part from increased MMP2 activity.

REFERENCE COUNT: 42
REFERENCE(S): (1) Barmina, O; J Biol Chem 1999, V274, P30087 HCAPLUS
(2) Bein, K; J Biol Chem 2000, V275, P32167 HCAPLUS
(3) Birkenmeier, G; Arch Dermatol Res 1998, V290, P561 HCAPLUS
(5) Bornstein, P; Matrix Biol 2000, V19, P557 HCAPLUS
(6) Bornstein, P; Methods Enzymol 1994, V245, P62 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 5 OF 35 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:131644 HCAPLUS
DOCUMENT NUMBER: 134:202760
TITLE: The role of VEGF and thrombospondins in **skin** angiogenesis
AUTHOR(S): Detmar, Michael
CORPORATE SOURCE: Department of Dermatology, Massachusetts General Hospital and Harvard, Cutaneous Biology Research Center, Charlestown, MA, 02129, USA
SOURCE: J. Dermatol. Sci. (2000), 24(Suppl. 1), S78-S84
CODEN: JDSCEI; ISSN: 0923-1811
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 30 refs. The vasculature in adult **skin** remains normally quiescent, due to the dominant influence of endogenous angiogenesis inhibitors over angiogenic stimuli. However, **skin** retains the capacity for brisk initiation of angiogenesis, the growth of new blood vessels from preexisting vessels, during tissue repair and in numerous diseases, including inflammatory **skin** diseases such as psoriasis and **skin cancers** such as cutaneous squamous cell **carcinomas**. Moreover, cyclic vascular expansion occurs during the growth phase of the hair follicle. Recent evidence suggests vascular endothelial growth factor as the major **skin** angiogenesis factor. During **skin** angiogenesis, expression of vascular endothelial growth factor is induced in **epidermal** keratinocytes by several stimuli including transforming growth

factor-.alpha. and hypoxia, leading to increased vascularization of the **dermis**. In contrast, vascular endothelial growth factor-C induces **skin** lymphangiogenesis. Thrombospondin-1 and **thrombospondin-2** are endogenous inhibitors of angiogenesis that are expressed in normal **skin**, maintaining the quiescence of cutaneous vessels. Both inhibitors potently inhibit **skin cancer** growth via inhibition of **tumor** angiogenesis. Targeting cutaneous blood vessels represents a promising new therapeutic approach for the treatment of a variety of **skin** diseases.

REFERENCE COUNT: 30
REFERENCE(S):
(1) Bornstein, P; FASEB J 1992, V6, P3290 HCAPLUS
(2) Bornstein, P; J Cell Biol 1995, V130, P503 HCAPLUS
(3) Carmeliet, P; Nat Med 2000, V6, P389 HCAPLUS
(4) Claffey, K; Mol Biol Cell 1998, V9, P469 HCAPLUS
(5) Connolly, D; J Clin Invest 1989, V84, P1470 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 6 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:103681 HCAPLUS
DOCUMENT NUMBER: 135:44240
TITLE: **Thrombospondin 2** modulates collagen fibrillogenesis and angiogenesis
AUTHOR(S): Bornstein, Paul; Kyriakides, Themis R.; Yang, Zhantao; Armstrong, Lucas C.; Birk, David E.
CORPORATE SOURCE: Department of Biochemistry, University of Washington, Seattle, WA, 98195, USA
SOURCE: J. Invest. Dermatol. Symp. Proc. (2000), 5(1), 61-66
CODEN: JDSPFO; ISSN: 1087-0024
PUBLISHER: Blackwell Science, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review, with 28 refs. **Thrombospondin 2** (TSP2)-null mice, generated by targeted disruption of the Thbs2 gene, display a complex phenotype that is characterized, in part, by a variety of connective tissue abnormalities and increased vascular d. in **skin** and s.c. tissues. In this paper we summarize the evidence that TSP2 functions as a matricellular protein to influence cell function by modulating cell-matrix interactions, rather than acting as an integral component of the matrix. Thus, the structurally abnormal collagen fibrils detected in **skin** appear to be the consequence of the defective adhesion demonstrated by **dermal** fibroblasts in culture that, in turn, result from increased matrix mmetalloproteinase 2 (MMP2, gelatinase A) prodn. by these cells. Corroborating evidence for such a mode of action comes from transmission electron microscopic images of developing flexor muscle tendons that show distinct abnormalities in fibroblast-collagen fibril interactions in TSP2-null tissue. The increased vascular d. seen in **skin** of TSP2-null mice can be reproduced in a no. of models of injury, including s.c. implantation of polyvinyl alc. sponges and silicone rubber disks, and excisional **skin** wounds. Expts. are proposed to distinguish between a primarily endothelial cell vs. an extracellular matrix origin for the increased angiogenesis in TSP2-null mice.

REFERENCE COUNT: 28
REFERENCE(S):
(1) Andrikopoulos, K; Nature Genet 1995, V9, P31 HCAPLUS
(2) Birk, D; Extracellular Matrix Assembly and Structure 1994, P91 HCAPLUS
(4) Bornstein, P; J Cell Biol 1995, V130, P503 HCAPLUS
(5) Bornstein, P; Meth Enzymol 1994, V245, P62 HCAPLUS
(6) Chen, H; J Biol Chem 1994, V269, P32226 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 7 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:103675 HCAPLUS

DOCUMENT NUMBER: 135:44234
TITLE: **Tumor** angiogenesis
AUTHOR(S): Detmar, Michael
CORPORATE SOURCE: Cutaneous Biology Research Center, Department of Dermatology, Massachusetts General Hospital and Harvard Medical School, Charlestown, MA, 02129, USA
SOURCE: J. Invest. Dermatol. Symp. Proc. (2000), 5(1), 20-23
CODEN: JDSPFO; ISSN: 1087-0024
PUBLISHER: Blackwell Science, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 56 refs. To grow beyond minimal size and to metastasize, **tumors** need to induce the growth of new blood vessels (angiogenesis). Whereas in normal tissues, vascular quiescence is maintained by the dominant influence of endogenous angiogenesis inhibitors over angiogenic stimuli, **tumor** angiogenesis is induced by increased secretion of angiogenic factors and/or by downregulation of angiogenesis inhibitors. Recent evidence suggests vascular endothelial growth factor (VEGF) as the major **tumor** angiogenesis factor, promoting **tumor** growth, invasion, and metastasis. Conversely, blocking of VEGF function inhibits angiogenesis and suppresses **tumor** growth in vivo. Newly identified members of the VEGF family of angiogenesis factors include placental growth factor, VEGF-B, VEGF-C, and VEGF-D, and show overlapping binding patterns to specific endothelial cell receptors. VEGF-C appears to play a major role as a lymphangiogenesis factor and as a growth factor for Kaposi's sarcoma. In contrast, endogenous inhibitors prevent blood vessel growth in normal tissues. In particular, thrombospondin-1 (TSP-1) and **TSP-2** are expressed in normal **skin** and, when introduced into squamous cell **carcinomas**, potently inhibit **malignant** **tumor** growth via inhibition of **tumor** angiogenesis.
REFERENCE COUNT: 56
REFERENCE(S): (1) Bornstein, P; FASEB J 1992, V6, P3290 HCAPLUS
(2) Bornstein, P; J Cell Biol 1995, V130, P503 HCAPLUS
(3) Bornstein, P; Proc Natl Acad Sci USA 1991, V88, P8636 HCAPLUS
(4) Brown, L; Exs 1997, V79, P233 HCAPLUS
(5) Campbell, S; Cancer Res 1998, V58, P1298 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 8 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:90683 HCAPLUS
DOCUMENT NUMBER: 135:32059
TITLE: Thrombospondin-1 and -2 in node-negative breast **cancer**: Correlation with angiogenic factors, p53, cathepsin D, hormone receptors and prognosis
AUTHOR(S): Gasparini, Giampietro; Toi, Masakazu; Biganzoli, Elia; Dittadi, Ruggero; Fanelli, Massimo; Morabito, Alessandro; Boracchi, Patrizia; Gion, Massimo
CORPORATE SOURCE: Division of Medical Oncology, Azienda Complesso Ospedaliero "San Filippo Neri", Rome, I-00135, Italy
SOURCE: Oncology (2001), Volume Date 2000, 60(1), 72-80
CODEN: ONCOBS; ISSN: 0030-2414
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Thrombospondins (TSPs) are a multigene family of five secreted glycoproteins involved in the regulation of cell proliferation, adhesion and migration. Two members of the TSP family, namely TSP-1 and **TSP-2**, are also naturally occurring inhibitors of angiogenesis. The aim of the present study was to det. the prognostic significance of the detn. of TSP-1 and -2 and their correlation with the angiogenic peptides vascular endothelial growth factor (VEGF) and thymidine phosphorylase (TP), as well as with other biol. and clinicopathol. features investigated. We evaluated a series of 168 women with node-neg. breast **cancer** with a median follow-up period of

66 mo, not treated with adjuvant therapy. The cytosolic levels of TSP-1 and -2 were detd. in the primary **tumor** by a com. available immunometric assay. We found that 166 tested **tumors** had measurable levels of TSP-1 and -2 protein (median value 5.978, range 0.579-31.410 ng/mg of protein). On the basis of Spearman's rank correlation coeff., a weak inverse assocn. of TSP-1 and -2 with **tumor** size and cathepsin D was found. Moreover, principal component anal. on ranks evidenced a poor assocn. between TSP-1 and -2, VEGF and TP. The results of the clin. outcome were analyzed by both univariate and multivariate [for relapse-free survival (RFS) only] Cox regression models. TSP-1 and -2 were not significant prognostic factors in univariate anal. for either RFS ($p = 0.427$) or overall survival ($p = 0.069$). To investigate the "angiogenic balance hypothesis", bivariate analyses were performed to investigate the interactions of TSP-1 and -2 with VEGF, TP or p53, but none were included in the selected models. Finally, in multivariate anal. for RFS a baseline model, previously defined in a larger case series and inclusive of VEGF, TP and their interaction was adopted. It was highly significant ($p = 0.002$, Harrell c statistic value of 0.703); but when TSP-1 and -2 were added, their contribution was negligible ($p = 0.731$, Harrell c statistic value of 0.705). The results of this.

REFERENCE COUNT: 48

REFERENCE(S):
(1) Baenziger, N; J Biol Chem 1972, V247, P2723 HCAPLUS
(2) Bertin, N; Cancer Res 1997, V57, P396 HCAPLUS
(4) Bornstein, P; Methods Enzymol 1994, V245, P62 HCAPLUS
(5) Clezardin, P; Cancer Res 1993, V53, P1421 HCAPLUS
(6) Crawford, S; Cell 1998, V93, P1159 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 9 OF 35 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:79956 HCAPLUS
DOCUMENT NUMBER: 135:44334

TITLE: Comparative study of angiostatic and anti-invasive gene expressions as prognostic factors in gastric **cancer**

AUTHOR(S): Lee, Ji Hee; Koh, Jeong Tae; Shin, Boo Ahn; Ahn, Kyu Youn; Roh, Jung Ho; Kim, Young Jin; Kim, Kyung Keun
CORPORATE SOURCE: Department of Surgery, Chonnam University Medical School, Kwangju, 501-190, S. Korea

SOURCE: Int. J. Oncol. (2001), 18(2), 355-361
CODEN: IJONES; ISSN: 1019-6439
PUBLISHER: International Journal of Oncology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Genes involving angiogenesis and metastasis play an important role in the progression and infiltration of **cancer**. The authors examd. the expressions of various angiostatic and potential invasion/metastasis suppressor genes through RT-PCR analyses in 32 gastric **cancer** specimens with or without distant metastasis. The expressions of the invasion/metastasis suppressor, nm23 and E-cadherin increased much more in the **cancer** tissue (CT) and metastatic lymph node (MLN) than in the **extraneoplastic** mucosa (EM) and non-metastatic lymph node (NLN), resp. The expressions of the angiostatic factor, angiopoietin 2 and **thrombospondin 2** increased in the CT and MLN as compared with the EM and NLN, resp. The newly cloned angiostatic factor, brain-specific angiogenesis inhibitor 1 (BAI1) decreased much more in the CT and MLN than the EM and NLN, resp. However, BAI1 increased in the CT compared with the EM among the patients with poor prognosis and distant metastasis, such as liver or peritoneum. The expressions of the invasive factor, matrix metalloproteinase-2 and its suppressor, tissue inhibitor metalloproteinase-2 (TIMP-2) increased in the CM as compared with the EM, but the increased expression pattern of these genes in the CT became blunted among the patients with good prognosis. These results indicate that BAI1 and TIMP-2 expressions in the **extraneoplastic** mucosa

and non-metastatic lymph nodes were not suppressed in the patients with good prognosis, but increased expressions of angiopoietin 2, **thrombospondin 2**, TIMP-2, nm23 and E-cadherin in the **tumor** tissue did not lead to a long survival after operation. It is suggested that the extent of BAI1 and TIMP-2 expression in the gastric mucosa may be an important prognostic factor for predicting survival in gastric **cancer**.

REFERENCE COUNT: 28
REFERENCE(S):
(4) Fridman, R; Biochem J 1993, V289, P411 HCAPLUS
(5) Fukushima, Y; Int J Oncol 1998, V13, P967 HCAPLUS
(6) Guilford, P; Mol Med Today 1999, V5, P172 HCAPLUS
(7) Hong, S; J Korean Med Sci 1996, V11, P474 HCAPLUS
(9) Iruela-Arispe, M; Circulation 1999, V100, P1423 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 10 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:15456 HCAPLUS
DOCUMENT NUMBER: 134:174295
TITLE: **Thrombospondin 2**, a matricellular protein with diverse functions
AUTHOR(S): Bornstein, Paul; Armstrong, Lucas C.; Hankenson, Kurt D.; Kyriakides, Themis R.; Yang, Zhantao
CORPORATE SOURCE: Department of Biochemistry, Department of Medicine, University of Washington, Seattle, WA, 98195, USA
SOURCE: Matrix Biol. (2000), 19(7), 557-568
CODEN: MTBOEC; ISSN: 0945-053X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB Thrombospondin (**TSP**) **2** is a close relative of TSP1 but differs in its temporal and spatial distribution in the mouse. A review with approx. 70 refs. This difference in expression undoubtedly reflects the marked disparity in the DNA sequences of the promoters in the genes encoding the two proteins. The synthesis of TSP2 occurs primarily in connective tissues of the developing and growing mouse. In the adult animal the protein is again produced in response to tissue injury and in assocn. with the growth of **tumors**. Despite the abnormalities in collagen fibrillogenesis, fragility of **skin**, and laxity of tendons and ligaments obsd. in the TSP2-null mouse, TSP2 does not appear to contribute directly to the structural integrity of connective tissue elements. Instead, emerging evidence supports a mode of action of TSP2 "at a distance", i.e. by modulating the activity and bioavailability of proteases and growth factors in the pericellular environment and, very likely, by interaction with cell-surface receptors. Thus, TSP2 qualifies as a matricellular protein, as defined in the introduction to this minireview series. The phenotype of TSP2-null mice has been very helpful in providing clues to the functions of TSP2. In addn. to histol. and functional abnormalities in connective tissues, these mice display an increased vascularity of the **dermis** and **subdermal** tissues, increased endosteal bone growth, a bleeding defect, and a marked adhesive defect of **dermal** fibroblasts. Our lab. has established that TSP2 binds matrix metalloproteinase 2 (MMP2) and that the adhesive defect in TSP2-null fibroblasts results from increased MMP2 activity. The investigation of the basis for the other defects in the TSP2-null mouse is likely to yield equally interesting results.

REFERENCE COUNT: 77
REFERENCE(S):
(1) Adolph, K; Biochem Biophys Res Commun 1999, V259, P527 HCAPLUS
(3) Beckstead, J; Blood 1986, V67, P285 HCAPLUS
(4) Bein, K; J Biol Chem 1998, V273, P21423 HCAPLUS
(5) Bornstein, P; FASEB J 1992, V6, P3290 HCAPLUS
(6) Bornstein, P; J Biol Chem 1990, V265, P16691 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 11 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:800665 HCAPLUS
DOCUMENT NUMBER: 134:125995
TITLE: Thrombospondin
AUTHOR(S): Kanda, Shigeru
CORPORATE SOURCE: Graduate School of Medicine, Nagasaki University, Japan
SOURCE: Kekkan Shinsei Kenkyu no Shintenkai (2000), 182-187. Editor(s): Murota, Seiitsu; Sato, Yasufumi. Iyaku Janarusha: Osaka, Japan. CODEN: 69APBF
DOCUMENT TYPE: Conference; General Review
LANGUAGE: Japanese
AB A review with 12 refs., on angiogenesis inhibitor action of thrombospondin (TSP), esp. TSP-1, discussing distribution and structure of TSP-1; relations between TSP-1 and growth factors; TSP-1 and **TSP-2** gene knockout mouse; effects of TSP-1 on angiogenesis; effects of TSP-1 domains and peptides on vascular endothelial cells; TSP-1 expression regulation and **tumor** suppressor genes; and application of TSP-1 in antiangiogenic therapy for **tumors**.

L28 ANSWER 12 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:771451 HCAPLUS
DOCUMENT NUMBER: 134:3040
TITLE: Matricellular proteins as modulators of cell-matrix interactions: adhesive defect in **thrombospondin 2**-null fibroblasts is a consequence of increased levels of matrix metalloproteinase-2
AUTHOR(S): Yang, Zhantao; Kyriakides, Themis R.; Bornstein, Paul
CORPORATE SOURCE: Department of Biochemistry, University of Washington, Seattle, WA, 98195, USA
SOURCE: Mol. Biol. Cell (2000), 11(10), 3353-3364
CODEN: MBCEEV; ISSN: 1059-1524
PUBLISHER: American Society for Cell Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Thrombospondin 2** (TSP2)-null mice, generated by disruption of the Thbs2 gene, display a variety of connective tissue abnormalities, including fragile **skin** and the presence of abnormally large collagen fibrils with irregular contours in **skin** and tendon. In this study we demonstrate that TSP2-null **skin** fibroblasts show a defect in attachment to a no. of matrix proteins, and a redn. in cell spreading. To investigate the mol. mechanisms responsible for these abnormal cell-matrix interactions, we compared the levels of matrix metalloproteinases (MMPs) in wild-type and mutant fibroblasts. Isolation and anal. of gelatinases from conditioned media by gelatin-agarose affinity chromatog. and gelatinolytic assays demonstrated that TSP2-null fibroblasts produce a 2-fold increase in gelatinase A (MMP2) compared with wild-type cells. The adhesive defect was cor. by treatment of TSP2-null fibroblasts with sol. TSP2, with the MMP inhibitors BB94 and tissue inhibitor of metalloproteinase-2, and with a neutralizing antibody to MMP2. Moreover, stable transfection of TSP2-null fibroblasts with mouse TSP2 cDNA cor. both the adhesive defect and the altered expression of MMP2. Finally, MMP2 was shown to interact with TSP2 in a direct-binding plate assay. We conclude that TSP2 plays an important role in cell-matrix interactions, and that a deficiency in the protein results in increased levels of MMP2 that contribute to the adhesive defect in TSP2-null fibroblasts and could play a role in the complex phenotype of TSP2-null mice.
REFERENCE COUNT: 47
REFERENCE(S): (3) Barmina, O; J Biol Chem 1999, V274, P30087 HCAPLUS
(5) Bian, J; Carcinogenesis 1996, V17, P1805 HCAPLUS
(6) Birk, D; Extracellular Matrix Assembly and Structure 1994, P91 HCAPLUS
(8) Bornstein, P; J Cell Biol 1995, V130, P503 HCAPLUS

(9) Bornstein, P; Methods Enzymol 1994, V245, P62 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 13 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:770966 HCAPLUS
DOCUMENT NUMBER: 134:268016
TITLE: The physical properties of leathers made from the **skins** of mice genetically deficient in decorin or **thrombospondin-2**
AUTHOR(S): Mozersky, S. M.; Iandola, S. K.; Liu, C. -K.; Phillips, J. G.; Marmer, W. N.; Eichstetter, I.; Iozzo, R. V.
CORPORATE SOURCE: Agricultural Research Service Eastern Regional Research Center, U.S. Department of Agriculture, Wyndmoor, PA, 19038-8598, USA
SOURCE: J. Am. Leather Chem. Assoc. (2000), 95(7), 229-235
CODEN: JALCAQ; ISSN: 0002-9726
PUBLISHER: American Leather Chemists Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The phys. properties of leathers made from the **skins** of mice genetically deficient in decorin or **thrombospondin-2** were compared to leathers made from the **skins** of control (normal) mice. Decorin deficiency was assocd. with a leather of significantly reduced tensile strength and stiffness. There was no evidence of a similar effect of **thrombospondin-2** deficiency. Neither deficiency had a significant effect on the extensibility of the **skin** or of leather produced from it. The implications of these findings are discussed.
REFERENCE COUNT: 19
REFERENCE(S): (1) Alexander, K; JALCA 1986, V81, P85 HCAPLUS
(3) Cabeza, L; JALCA 1998, V93, P83 HCAPLUS
(4) Chakravarti, S; J Cell Biol 1998, V141, P1277 HCAPLUS
(5) Colige, A; Proc Natl Acad Sci 1997, V94, P2374 HCAPLUS
(7) Danielson, K; J Cell Biol 1997, V136, P729 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 14 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:717968 HCAPLUS
DOCUMENT NUMBER: 134:40277
TITLE: Angiogenesis Modulators Expression in Culture Cell Lines Positives for HPV-16 Oncoproteins
AUTHOR(S): Bequet-Romero, Monica; Lopez-Ocejo, Omar
CORPORATE SOURCE: Pharmaceutical Division, Centre for Genetic Engineering and Biotechnology, Havana, 10600, Cuba
SOURCE: Biochem. Biophys. Res. Commun. (2000), 277(1), 55-61
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Altered angiogenesis response is obsd. in patients with cervical **cancer**. In this study we examd. whether Human Papilloma Virus (HPV) pos. epithelial cells are able to produce angiogenic modulators. When added to human umbilical vein endothelial cells (HUVEC) the media conditioned by HPV-16 pos. cells was able to induce proliferation, whereas a contrary effect was obsd. for media derived from non-**tumorigenic** keratinocytes. The analyses of angiogenesis modulator's mRNA levels result in a decrease of the antiangiogenic factors TSP-1 and 2 in HPV-16 pos. cells. In contrast the expression of the pro-angiogenic mols.: bFGF, IL-8, TGF-.beta., TNF.alpha., and VEGF were higher in these cells as compared to control keratinocytes. Furthermore the pattern of VEGF isoforms obsd. in the cells pos. for the viral genome point to a preferential induction of the VEGF189 isoform. We therefore conclude that

cervical **cancer** cells expressing HPV-16 genome are able to contribute to the pro-angiogenic response that might support **tumor** growth and invasion of the surrounding tissues. (c) 2000 Academic Press.

REFERENCE COUNT: 44

REFERENCE(S):
(1) Arbeit, J; Oncogene 1996, V13, P1847 HCAPLUS
(3) Boukamp, P; J Cell Biol 1988, V106, P761 HCAPLUS
(4) Brown, K; Lab Invest 1996, V75, P539 HCAPLUS
(5) Chomczynski, P; Anal Biochem 1987, V162, P156 HCAPLUS
(7) Dameron, K; Science 1994, V265, P1582 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 15 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:707001 HCAPLUS
DOCUMENT NUMBER: 133:276326
TITLE: **Thrombospondin-2** for control of angiogenesis and unwanted cell proliferation
INVENTOR(S): Detmar, Michael; Streit, Michael
PATENT ASSIGNEE(S): The General Hospital Corp., USA
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000057899	A1	20001005	WO 2000-US7835	20000324

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-127221 P 19990331

AB The invention features a method of treating a disorder characterized by unwanted angiogenesis and/or unwanted cellular proliferation, e.g., unwanted **skin** or prostate cell proliferation, by increasing a **TSP-2** activity. The invention also features methods of identifying compds. which modulate, e.g., inhibit or promote, **TSP -2** activity, and methods of evaluating if a subject is at risk for a disorder characterized by unwanted angiogenesis and/or unwanted cellular proliferation. The invention also features fragments and analogs of **TSP-2** which can be used to treat such disorders.

IT **299491-48-8P, Thrombospondin-2 (human clone pSecTag)**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(amino acid sequence; **thrombospondin-2** for control of angiogenesis and unwanted cell proliferation)

REFERENCE COUNT: 1

REFERENCE(S):
(1) Streit; Proceedings of the National Academy of Sciences of the United States of America 1999, V96(26), P14888 HCAPLUS

L28 ANSWER 16 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:535287 HCAPLUS
DOCUMENT NUMBER: 133:145901
TITLE: COMP/TSP-1, COMP/**TSP-2** and other chimeric proteins as angiogenesis and HIV inhibitor

INVENTOR(S): Lawler, John W.
PATENT ASSIGNEE(S): Beth Israel Deaconess Medical Center, USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000044908	A2	20000803	WO 2000-US2482	20000201
WO 2000044908	A3	20010215		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-118053 P 19990201

AB **Tumors** attract blood vessels in order to grow by a process called angiogenesis. The relative quantity of stimulators and inhibitors is an important detg. factor for the initiation of angiogenesis. Thrombospondins-1 and -2 are adhesive glycoproteins that have the ability to inhibit angiogenesis. This inhibiting activity has been mapped to the type 1 repeats of TSP-1 and **TSP-2**. The invention includes chimeric proteins that contain anti-angiogenic portions of TSP-1, **TSP-2**, endostatin, angiostatin, platelet factor 4, or prolactin, linked to a portion of the N-terminal region of human cartilage oligomeric matrix protein (COMP) that allows formation of pentamers. Also described herein are the nucleic acid mols., vectors, and host cells for expressing and producing these chimeric proteins. Further embodiments of the invention include methods to treat humans or other mammals with anti-angiogenic proteins to reduce **tumor** size or rate of growth. Since the type 1 repeat region of TSP-1 and **TSP-2** reportedly inhibits HIV infection, chimeric proteins comprising these repeats may also be used for this purpose, as well as to inhibit angiogenesis.

L28 ANSWER 17 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:145067 HCAPLUS
DOCUMENT NUMBER: 132:206569
TITLE: Expression monitoring for human cytomegalovirus (HCMV) infection, and genes possibly involved in mediating the pathology of HCMV infection
INVENTOR(S): Zhu, Hua; Gingeras, Thomas; Shenk, Thomas
PATENT ASSIGNEE(S): Affymetrix, Inc., USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000011218	A1	20000302	WO 1999-US18772	19990820

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9956776 A1 20000314 AU 1999-56776 19990820

PRIORITY APPLN. INFO.: US 1998-97708 P 19980821
WO 1999-US18772 W 19990820

AB The invention provides methods, compns., and app. for studying the complex regulatory relationships among host genes and viruses, in particular HCMV. The invention also provides cellular mRNAs whose levels change by a factor of four or more after infection with HCMV. Such genes are likely those involved in mediating the pathol. of the infected tissues. Thus by identifying agents which are able to reverse the induction or repression of such genes, one can find candidate therapeutic agents for use in treating and or preventing HCMV-caused disease pathologies.

REFERENCE COUNT: 12

REFERENCE(S):
(1) Boldogh; Proceedings of the Society for Experimental Biology and Medicine V215(1), P66 HCAPLUS
(2) Chee; US 5795716 1998 HCAPLUS
(3) Colberg-Poley; Virology 1988, V166, P217 HCAPLUS
(4) Geist; Journal of Clinical Investigation 1994, V93, P474 HCAPLUS
(5) Geist; Transplantation 1996, V62(5), P653 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 18 OF 35 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:14359 HCAPLUS

DOCUMENT NUMBER: 132:249290

TITLE: Expression of angiostatic factors in colorectal **cancer**

AUTHOR(S): Yoshida, Yukiko; Oshika, Yoshiro; Fukushima, Yoshitaka; Tokunaga, Tetsuji; Hatanaka, Hiroyuki; Kijima, Hiroshi; Yamazaki, Hitoshi; Ueyama, Yoshito; Tamaoki, Norikazu; Miura, Soichiro; Nakamura, Masato

CORPORATE SOURCE: Department of Pathology, Tokai University School of Medicine, Kanagawa, 259-1193, Japan

SOURCE: Int. J. Oncol. (1999), 15(6), 1221-1225
CODEN: IJONES; ISSN: 1019-6439

PUBLISHER: International Journal of Oncology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Angiogenesis plays an important role in growth and proliferation of **cancer**. Various angiogenic and angiostatic factors regulate angiogenesis. The authors examd. expression of genes encoding various angiostatic factors: thrombospondin 1 (TSP1), **thrombospondin 2** (TSP2), brain-specific angiogenesis inhibitor 1 (BAI1) and angiopoietin 2 (AGP2) in 62 colorectal **cancers** and 40 samples of **extraneoplastic** colon mucosa. The expression of the angiostatic factors TSP2 and AGP2 were significantly increased in the **cancerous** mucosa as compared to these in **extraneoplastic** mucosa, while the increase in TSP1 expression was not significant. BAI1 expression was slightly decreased in the **cancer** tissue. These results suggested that specific types of angiostatic factors might have protective roles against **cancer** cell proliferation via dormancy due to hyponutrition caused by decreased vascularity.

REFERENCE COUNT: 40

REFERENCE(S):
(1) Berkman, R; J Clin Invest 1993, V91, P153 HCAPLUS
(2) Boocock, C; J Natl Cancer Inst 1995, V87, P506 HCAPLUS
(4) Davis, S; Cell 1996, V87, P1161 HCAPLUS
(5) Dumont, D; Genes Dev 1994, V8, P1897 HCAPLUS
(6) Dumont, D; Oncogene 1992, V7, P1471 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 19 OF 35 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:11248 HCAPLUS

DOCUMENT NUMBER: 132:149957
TITLE: **Thrombospondin-2**: a potent endogenous inhibitor of **tumor** growth and angiogenesis
AUTHOR(S): Streit, Michael; Riccardi, Lucia; Velasco, Paula; Brown, Lawrence F.; Hawighorst, Thomas; Bornstein, Paul; Detmar, Michael
CORPORATE SOURCE: Cutaneous Biology Research Center and Department of Dermatology, Massachusetts General Hospital and Harvard Medical School, Charlestown, MA, 02129, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1999), 96(26), 14888-14893
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

Applicant's own work

AB Recent evidence suggests a potential role for **thrombospondin-2** (**TSP-2**), a matricellular glycoprotein, in the regulation of primary angiogenesis. To directly examine the biol. effect of **TSP-2** expression on **tumor** growth and angiogenesis, human A431 squamous cell **carcinoma** cells, which do not express **TSP-2**, were stably transfected with a murine **TSP-2** expression vector or with vector alone. A431 cells expressing **TSP-2** did not show an altered growth rate, colony-forming ability, or susceptibility to induction of apoptosis in vitro. However, injection of **TSP-2**-transfected clones into the **dermis** of nude mice resulted in pronounced inhibition of **tumor** growth that was significantly stronger than the inhibition obsd. in A431 clones stably transfected with a thrombospondin-1 (TSP-1) expression vector, and combined overexpression of TSP-1 and **TSP-2** completely prevented **tumor** formation. Extensive areas of necrosis were obsd. in **TSP-2**-expressing **tumors**, and both the d. and the size of **tumor** vessels were significantly reduced, although **tumor** cell expression of the major **tumor** angiogenesis factor, vascular endothelial growth factor, was maintained at high levels. These findings establish **TSP-2** as a potent endogenous inhibitor of **tumor** growth and angiogenesis.

REFERENCE COUNT: 41
REFERENCE(S):
(1) Adams, J; Curr Biol 1993, V3, P188 HCAPLUS
(2) Bergers, G; Science 1999, V284, P808 HCAPLUS
(3) Berse, B; Mol Biol Cell 1992, V3, P211 HCAPLUS
(4) Bertin, N; Cancer Res 1997, V57, P396 HCAPLUS
(5) Bleuel, K; Proc Natl Acad Sci USA 1999, V96, P2065 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 20 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:763372 HCAPLUS
DOCUMENT NUMBER: 132:76690
TITLE: Accelerated wound healing in mice with a disruption of the **thrombospondin 2** gene
AUTHOR(S): Kyriakides, Themis R.; Tam, Jessica W. Y.; Bornstein, Paul
CORPORATE SOURCE: Department of Biochemistry, University of Washington, Seattle, WA, 98195, USA
SOURCE: J. Invest. Dermatol. (1999), 113(5), 782-787
CODEN: JIDEAE; ISSN: 0022-202X
PUBLISHER: Blackwell Science, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Mice that lack the extracellular matrix protein **thrombospondin 2** have, among several abnormalities, an increase in vascular d., abnormal collagen fibrils, and **dermal** fibroblasts that are defective in adhesion. These findings suggested that responses involving these processes, such as wound healing, might be altered. To investigate

the healing process, excisional wounds were made with the aid of a biopsy punch. Such wounds, obsd. over a 14 day period, appeared to heal at an accelerated rate and with less scarring in **thrombospondin 2**-null mice. Histol. anal. of **thrombospondin 2**-null wound sites revealed the presence of an irregularly organized and highly vascularized granulation tissue. In addn., **thrombospondin 2**-null wounds retained a higher total cellular content, than control wounds. No differences in wound re-epithelization rates were obsd., but **thrombospondin 2**-null epithelia formed rete pegs and were thicker than control epithelia. By immunohistochem., we detected elevated levels and an irregular deposition pattern for fibronectin in **thrombospondin 2**-null wounds, observations that correlated with the abnormal collagen organization in the granulation tissue. Immunostaining for **thrombospondin 2** in control wounds showed that the protein is present in both early and late wounds, in a scattered cell-assocd. pattern or widely distributed cell- and matrix-assocd. pattern, resp. Our results suggest that **thrombospondin 2** plays a crucial part in the organization and vascularization of the granulation tissue during healing, possibly by modulating fibroblast-matrix interactions in early wounds and regulating the extent of angiogenesis in late wounds.

REFERENCE COUNT: 32
REFERENCE(S):
(1) Adams, J; J Cell Sci 1993, V104, P1061 HCAPLUS
(3) Bornstein, P; FASEB J 1992, V6, P3290 HCAPLUS
(4) Bornstein, P; J Cell Biol 1995, V130, P503 HCAPLUS
(5) Bornstein, P; Methods Enzymol 1994, V245, P62 HCAPLUS
(8) DiPietro, L; Am J Pathol 1996, V148, P1851 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 21 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:368612 HCAPLUS
DOCUMENT NUMBER: 131:143072
TITLE: Mice that lack the angiogenesis inhibitor, **thrombospondin 2**, mount an altered foreign body reaction characterized by increased vascularity
AUTHOR(S): Kyriakides, Themis R.; Leach, Kathleen J.; Hoffman, Allan S.; Ratner, Buddy D.; Bornstein, Paul
CORPORATE SOURCE: Department of Biochemistry, University of Washington, Seattle, WA, 98195, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1999), 96(8), 4449-4454
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Disruption of the **thrombospondin 2** gene (Thbs2) in mice results in a complex phenotype characterized chiefly by abnormalities in fibroblasts, connective tissues, and blood vessels. Consideration of this phenotype suggested to the authors that the foreign body reaction (FBR) might be altered in **thrombospondin 2** (TSP2)-null mice. To investigate the participation of TSP2 in the FBR, polydimethylsiloxane (PDMS) and oxidized PDMS (ox-PDMS) disks were implanted in TSP2-null and control mice. Growth of TSP2-null and control **skin** fibroblasts in vitro also was evaluated on both types of disks. Normal fibroblasts grew as a monolayer on both surfaces, but attachment of the cells to ox-PDMS was weak and sensitive to movement. TSP2-null fibroblasts grew as aggregates on both surfaces, and their attachment was further compromised on ox-PDMS. After a 4-wk implantation period, both types of PDMS elicited a similar FBR with a collagenous capsule in both TSP2-null and control mice. However, strikingly, the collagenous capsule that formed in TSP2-null mice was highly vascularized and thicker than that formed in normal mice. In addn., abnormally shaped collagen fibers were obsd. in capsules from mutant mice. Thus, the presence or absence of an extracellular matrix component, TSP2, can

influence the nature of the FBR, in particular its vascularity. The expression of TSP2 therefore could represent a mol. target for local inhibitory measures when vascularization of the tissue surrounding an implanted device is desired.

REFERENCE COUNT: 37

REFERENCE(S):
(1) Altankov, G; J Biomed Mat Res 1996, V30, P385 HCAPLUS
(4) Bohnert, J; J Colloid Interface Sci 1986, V111, P363 HCAPLUS
(6) Brauker, J; J Biomed Mater Res 1995, V29, P1517 HCAPLUS
(7) Crawford, S; Cell 1998, V93, P1159 HCAPLUS
(8) den Braber, E; J Biomed Mater Res 1997, V37, P539 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 22 OF 35 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:245923 HCAPLUS

DOCUMENT NUMBER: 131:86150

TITLE: **Thrombospondin-2** (TSP2) expression is inversely correlated with vascularity in glioma

AUTHOR(S): Kazuno, M.; Tokunaga, T.; Oshika, Y.; Tanaka, Y.; Tsugane, R.; Kijima, H.; Yamazaki, H.; Ueyama, Y.; Nakamura, M.

CORPORATE SOURCE: Department of Neurosurgery, School of Medicine, Tokai University, Kanagawa, 259-1193, Japan

SOURCE: Eur. J. Cancer (1999), 35(3), 502-506
CODEN: EJCAEL; ISSN: 0959-8049

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Thrombospondins (TSPs) are angiostatic factors in various **cancers**. However, the significance of TSPs has not been well characterized in glioma. We examd. TSP1, TSP2 and vascular endothelial growth factor (VEGF) gene expression by reverse transcription-polymerase chain reaction (RT-PCR) in 37 gliomas. Thirty of the 37 glioma specimens showed VEGF gene expression. Eighteen of the 37 gliomas expressed the TSP1 gene. Seven gliomas lacked TSP2 gene expression, while the other 30 expressed TSP2. The lack of TSP2 gene expression was significantly assocd. with higher histol. grade (Fisher's test, P=0.0019) and increased vessel counts and d. (Student's t-test, P<0.0001), while there were no correlations between TSP1 and VEGF gene expression and clinicopathol. features. These results indicate that the lack of TSP2 gene expression is a potent factor for enhancement of angiogenesis in glioma.

REFERENCE COUNT: 30

REFERENCE(S):
(1) Baenziger, N; J Biol Chem 1972, V247, P2723 HCAPLUS
(2) Bornstein, P; FASEB J 1992, V6, P3290 HCAPLUS
(3) Bornstein, P; J Biol Chem 1991, V266, P12821 HCAPLUS
(7) Grossfeld, G; J Natl Cancer Inst 1997, V89, P219 HCAPLUS
(8) Hsu, S; Cancer Res 1996, V56, P5684 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 23 OF 35 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:69340 HCAPLUS

DOCUMENT NUMBER: 130:280015

TITLE: **Thrombospondin 2** expression is correlated with inhibition of angiogenesis and metastasis of colon **cancer**

AUTHOR(S): Tokunaga, T.; Nakamura, M.; Oshika, Y.; Abe, Y.; Ozeki, Y.; Fukushima, Y.; Hatanaka, H.; Sadahiro, S.; Kijima, H.; Tsuchida, T.; Yamazaki, H.; Tamaoki, N.; Ueyama, Y.

CORPORATE SOURCE: Department of Pathology, Tokai University School of

Medicine, Kanagawa, 259-1193, Japan
SOURCE: Br. J. Cancer (1999), 79(2), 354-359
CODEN: BJCAAI; ISSN: 0007-0920
PUBLISHER: Churchill Livingstone
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two subtypes of thrombospondin (TSP-1 and **TSP-2**) have inhibitory roles in angiogenesis in vitro, although the biol. significance of these TSP isoforms has not been detd. in vivo. The authors examd. TSP-1 and **TSP-2** gene expression by reverse transcription polymerase chain reaction (RT-PCR) anal. in 61 colon **cancers**. Thirty-eight of these 61 colon **cancers** were pos. for **TSP-2** expression and showed hepatic metastasis at a significantly lower incidence than those without **TSP-2** expression. **TSP-2** expression was significantly assocd. with MO stage in these colon **cancers**, whereas TSP-1 expression showed no apparent correlation with these factors. The colon **cancer** patients with **TSP-2** expression showed a significantly low frequency of liver metastasis correlated with the cell-assocd. isoform of vascular endothelial growth factor (VEGF-189). Vascularity was estd. by CD34 staining, and **TSP-2**(-)/VEGF-189(+) colon **cancers** showed significantly increased vessel counts and d. in the stroma. **TSP-2**(-)/VEGF-189(+) colon **cancer** patients also showed significantly poorer prognosis compared with those with **TSP-2**(+) / VEGF-189(-). These results suggest that colon **cancer** metastasis is critically detd. by angiogenesis resulting from the balance between the angioinhibitory factor **TSP-2** and angiogenic factor VEGF-189.
REFERENCE COUNT: 45
REFERENCE(S): (1) Baenziger, N; J Biol Chem 1972, V247, P2723 HCAPLUS
(2) Bertin, N; Cancer Res 1997, V57, P396 HCAPLUS
(3) Bornstein, P; FASEB J 1992, V6, P3290 HCAPLUS
(4) Bornstein, P; J Biol Chem 1991, V266, P12821 HCAPLUS
(5) Clezardin, P; Cancer Res 1993, V53, P1421 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 24 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:642253 HCAPLUS
DOCUMENT NUMBER: 130:64379
TITLE: **Tumor** vasculature and angiogenic factors
AUTHOR(S): Toi, Masakazu; Ueno, Takayuki
CORPORATE SOURCE: Dep. Surg., Tokyo Metrop. Komagome Gen. Hosp., Tokyo, 113-8677, Japan
SOURCE: Mol. Med. (Tokyo) (1998), 35(10), 1232-1241
CODEN: MOLMEL; ISSN: 0918-6557
PUBLISHER: Nakayama Shoten
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review with 33 refs. Angiogenesis is regulated by subtle balance of pos. and neg.-regulating factors, and neg.-regulating factors of angiostatin and endostatin are the fragments of endogenous proteins. The balance of proteases and their inhibitors are also important for angiogenesis. Host cells of macrophages (**tumor** assocd. macrophages, TAM), mast cells and fibroblasts penetrating **tumor** stroma play important roles in angiogenesis by secreting various factors such as vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF). The relation of angiogenesis-relating factors to microvessel d. (MVD) and **tumor** prognosis is listed. The **intratumor** level of bFGF does not correlate with MVD but is a prognosis factor (PF) in primary breast **cancer**. VEGF exhibits pos. correlation with acceleration of angiogenesis in various **tumor**, and is the PF for breast **cancer**, gastric **cancer**, esophagus **cancer**, colon **cancer** and

bowel **cancer**. The blood level of VEGF increases in **tumor** patients, esp. with advanced **cancer** and high VEGF **cancer**. Thymidine phosphorylase (TP) exhibits pos. correlation to MVD in breast **cancer**, colon, **cancer**, gastric **cancer** and lung **cancer**. TP is the PF for various **cancers**, esp. in colon **cancer**. Hepatocyte growth factor (HGF) is the PF for breast **cancer** and shows pos. correlation with MVD in uterus **cancer**. The expression of tyrosine kinase with Ig and EGF homol. domain-2 (Tie-2) is elevated in breast **cancer**. **Thrombospondin 2** (**TSP-2**) exhibits neg. correlation with MVD in non-small cell lung **carcinoma**. Adrenomedullin is induced by tamoxifen, and induces angiogenesis in uterus.

L28 ANSWER 25 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:622884 HCAPLUS
DOCUMENT NUMBER: 129:342208
TITLE: Stress-induced secretion of growth inhibitors: a novel **tumor** suppressor function of p53
AUTHOR(S): Komarova, Elena A.; Diatchenko, Luda; Rokhlin, Oskar W.; Hill, Jason E.; Wang, Zhaohui J.; Krivokrysenko, Vadim I.; Feinstein, Elena; Gudkov, Andrei V.
CORPORATE SOURCE: Department of Molecular Genetics, College of Medicine, University of Illinois at Chicago, Chicago, IL, 60607, USA
SOURCE: Oncogene (1998), 17(9), 1089-1096
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB P53 **tumor** suppressor gene controls cell response to a variety of stresses inducing growth arrest or apoptosis in damaged cells. It largely dets. the sensitivity of **tumor** and normal cells to radiation and chemotherapy, and, therefore, defines both the efficacy and limitations of anti-**cancer** treatment. To det. mol. mechanisms of p53-dependent stress response in normal tissues we identified and compared the spectra of radiation-responsive genes in cells of different origin and p53 status using a cDNA array hybridization technique. The majority of genes identified were p53-dependent and cell type specific. Several of the new p53 responders encode known secreted growth inhibitory factors. This suggests that p53, in addn. to its intrinsic antiproliferation activity, can cause "bystander effect" by inducing export of growth suppressive stimuli from damaged cells to neighboring cells. Consistently, a p53-dependent accumulation of factors, which causes growth inhibitory effects in a variety of cell lines, was found after gamma irradn. in the media from established and primary cell cultures and in the urine of irradiated mice. Moreover, p53-dependent factors released by normal human fibroblasts potentiated the cytotoxic effect of a chemotherapeutic drug on co-cultivated **tumor** cells. This suggests a previously unknown role for normal cells in chemo- and radiation therapy of **cancer**.

L28 ANSWER 26 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:586930 HCAPLUS
DOCUMENT NUMBER: 129:300449
TITLE: The distribution of the matricellular protein **thrombospondin 2** in tissues of embryonic and adult mice
AUTHOR(S): Kyriakides, Themis R.; Zhu, Yu-Hong; Yang, Zhantao; Bornstein, Paul
CORPORATE SOURCE: Dep. Biochem., Univ. Washington, Seattle, WA, 98195, USA
SOURCE: J. Histochem. Cytochem. (1998), 46(9), 1007-1015
CODEN: JHCYAS; ISSN: 0022-1554
PUBLISHER: Histochemical Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Mice that lack the matricellular protein **thrombospondin 2** (TSP2) develop a pleiotropic phenotype characterized by morphol. changes in connective tissues, an increase in vascular d., and a propensity for bleeding. Furthermore, **dermal** cells derived from TSP2-null mice display adhesion defects, a finding that implicates TSP2 in cell-matrix interactions. To gain a better understanding of the participation of TSP2 in the development and maturation of the mouse, we examd. its distribution in embryonic and adult tissues. Special attention was paid to the presence of TSP2 in collagen fibers, because collagen fibrils in the TSP2-null mouse appear to be irregular in size and contour by electron microscopy. Immunohistochem. anal. of Day 15 and Day 18 embryos revealed TSP2 in areas of chondrogenesis, osteogenesis, and vasculogenesis, and in **dermal** and other connective tissue-forming cells. Distinctly different patterns of deposition of TSP2 were obsd. in areas of developing cartilage and bone at Day 15 and 18 of embryonic development. A survey of adult tissues revealed TSP2 in **dermal** fibroblasts, articular chondrocytes, Purkinje cells in the cerebellum, Leydig cells in the testis, and in the adrenal cortex. **Dermal** fibroblasts were also shown to synthesize TSP2 in vitro. The distribution of TSP2 during development is in keeping with its participation in the formation of a variety of connective tissues. In adult tissues, TSP2 is located in the pericellular environment, where it can potentially influence the cell-matrix interactions assocd. with cell movement and tissue repair.

L28 ANSWER 27 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:466171 HCAPLUS
DOCUMENT NUMBER: 129:229002
TITLE: **Thrombospondin 2** gene expression is correlated with decreased vascularity in non-small cell lung **cancer**
AUTHOR(S): Oshika, Yoshiro; Masuda, Keiko; Tokunaga, Tetsuji; Hatanaka, Hiroyuki; Kamiya, Takashi; Abe, Yoshiyuki; Ozeki, Yuichi; Kijima, Hiroshi; Yamazaki, Hitoshi; Tamaoki, Norikazu; Ueyama, Yoshito; Nakamura, Masato
CORPORATE SOURCE: Department of Pathology, Tokai University School of Medicine, Kanagawa, 259-1193, Japan
SOURCE: Clin. Cancer Res. (1998), 4(7), 1785-1788
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Stromal vascularity is thought to be a major factor involved in the progression of **carcinoma**. However, the crucial mechanisms of vascularization in the stroma are not well understood. Vascularity could be regulated by various cytokines produced by **neoplastic** or stromal cells in **carcinoma**. Thrombospondin (TSP) has an inhibitory role against vascularization in vitro, although the biol. significance of TSP has not been characterized in vivo. We examd. expression of TSP1 and TSP2 genes in 78 non-small cell lung **cancers** (NSCLCs) and 33 **extraneoplastic** lung tissue samples by reverse transcription-PCR. TSP1 expression was detected in 66.7% (52 of 78) of NSCLCs and in 69.7% (23 of 33) of **extraneoplastic** lung tissue specimens. TSP2 expression was seen in 48.7% (38 of 78) of NSCLCs, whereas 72.7% (24 of 33) of **extraneoplastic** lung tissue samples showed TSP2 gene expression. TSP2 expression was significantly decreased in NSCLC as compared with **extraneoplastic** lung tissue (.chi.2 test, P = 0.019). Vascularity in the NSCLC was inversely correlated with TSP2 gene expression (Mann-Whitney U test, P = 0.009). Patients with **adenocarcinoma** pos. for TSP2 gene expression (22 of 49) showed significantly better prognosis than those without TSP2 (27 of 49; Cox-Mantel test, P = 0.034). TSP1 expression showed no apparent correlation with these factors. These results suggested that TSP2 had an inhibitory role against vascularization and progression of NSCLC.

L28 ANSWER 28 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:427481 HCAPLUS
DOCUMENT NUMBER: 129:159614
TITLE: Restricted localization of **thrombospondin-2** protein during mouse embryogenesis: a comparison to thrombospondin-1
AUTHOR(S): Tooney, Paul A.; Sakai, Takao; Sakai, Keiko; Aeschlimann, Daniel; Mosher, Deane F.
CORPORATE SOURCE: Departments of Medicine and Biomolecular Chemistry, University of Wisconsin-Madison, Madison, WI, USA
SOURCE: Matrix Biol. (1998), 17(2), 131-143
CODEN: MTBOEC; ISSN: 0945-053X
PUBLISHER: Gustav Fischer Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Thrombospondin-1 and -2 (TSP1 and TSP2) are multifunctional, multimodular extracellular matrix proteins encoded by sep. genes. Here, the authors compared the distributions of TSP1 and TSP2 in mouse embryos (day 10 and later) by immunohistochem. TSP1 was detected on day 10 in the heart and intestinal epithelium, on day 11 in megakaryocytes, and on day 14 in the lung. TSP2 was not detected until day 14, with strongest staining in mesenchymal condensation that gives rise to cartilage and bone. The distribution of TSP2 was different from but overlapped with the distribution of TSP1. TSP1 was found in cartilage proper with diminished staining around chondrocytes undergoing differentiation and hypertrophy, whereas TSP2 was restricted to the matrix surrounding chondrocytes of the growth zone cartilage. TSP2 and TSP1 were both expressed in centers of intramembranous ossification that form the skull bones, in reticular **dermis**, on the apical surface of nasal epithelium, in skeletal muscle, and in the sheath surrounding vibrissae. Areas of exclusive staining for TSP2 included the perichondrium surrounding the cartilage of the nasal cavities, developing bone of the lower mandible, and adrenal gland. The distinct localizations of TSP1 and TSP2 indicate that the 2 proteins have specific functions during mouse embryogenesis.

L28 ANSWER 29 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:64937 HCAPLUS
DOCUMENT NUMBER: 128:203360
TITLE: Mice that lack **thrombospondin 2** display connective tissue abnormalities that are associated with disordered collagen fibrillogenesis, an increased vascular density, and a bleeding diathesis
AUTHOR(S): Kyriakides, Themis R.; Zhu, Yu-Hong; Smith, Lynne T.; Bain, Steven D.; Yang, Zhantao; Lin, Ming T.; Danielson, Keith G.; Iozzo, Renato V.; Lamarca, Mary; Mckinney, Cindy E.; Ginns, Edward I.; Bornstein, Paul
CORPORATE SOURCE: Department of Biochemistry, University of Washington, Seattle, WA, 98195, USA
SOURCE: J. Cell Biol. (1998), 140(2), 419-430
CODEN: JCLBA3; ISSN: 0021-9525
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Thrombospondin (**TSP**) **2**, and its close relative TSP1, are extracellular proteins whose functions are complex, poorly understood, and controversial. In an attempt to det. the function of TSP2, we disrupted the Thbs2 gene by homologous recombination in embryonic stem cells, and generated TSP2-null mice by blastocyst injection and appropriate breeding of mutant animals. Thbs2-/- mice were produced with the expected Mendelian frequency, appeared overtly normal, and were fertile. However, on closer examn., these mice displayed a wide variety of abnormalities. Collagen fiber patterns in **skin** were disordered, and abnormally large fibrils with irregular contours were obsd. by electron microscopy in both **skin** and tendon. As a functional correlate of these findings, the **skin** was fragile and

had reduced tensile strength, and the tail was unusually flexible. Mutant **skin** fibroblasts were defective in attachment to a substratum. An increase in total d. and in cortical thickness of long bones was documented by histol. and quant. computer tomog. Mutant mice also manifested an abnormal bleeding time, and histol. surveys of mouse tissues, stained with an antibody to von Willebrand factor, showed a significant increase in blood vessels. The basis for the unusual phenotype of the TSP2-null mouse could derive from the structural role that TSP2 might play in collagen fibrillogenesis in **skin** and tendon. However, it seems likely that some of the diverse manifestations of this genetic disorder result from the ability of TSP2 to modulate the cell surface properties of mesenchymal cells, and thus, to affect cell functions such as adhesion and migration.

L28 ANSWER 30 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:142793 HCAPLUS
DOCUMENT NUMBER: 126:234913
TITLE: Identification of cell adhesive active sites in the N-terminal domain of thrombospondin-1
AUTHOR(S): Clezardin, Philippe; Lawler, Jack; Amiral, Jean; Quentin, Gerard; Delmas, Pierre
CORPORATE SOURCE: INSERM Research Unit 403, Hopital Edouard Herriot, Lyon, 69437, Fr.
SOURCE: Biochem. J. (1997), 321(3), 819-827
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Using a series of fusion proteins that span almost all of the thrombospondin-1 (TSP-1) mol., we obsd. in this study that Chinese hamster ovary (CHO) K1 cells strongly attached to the N-terminus but not to the other domains of TSP-1 (e.g. the C-terminus, and type 1, type 2, and type 3 repeats). In addn., attachment to the N-terminus of CHO S745 cells defective in cell-surface glycosaminoglycans (GAGs) was decreased by 47% compared with that obsd. with CHO K1 cells, indicating the presence of GAG-dependent cell adhesive sites. With the aim of identifying these cell adhesive sites, a series of synthetic peptides, overlapping heparin-binding sequences ARKGSGRR (residues 22-29), MKKTRG (residues 79-84), and TRDLASIARLRIAKGVNDNF (residues 170-189), were synthesized and tested for their ability to support CHO cell attachment. Using both centrifugation and cell-attachment assays, MKKTRG-contg. peptides promoted CHO K1 cell adhesion, while ARKGSGRR-contg. peptides and peptide TRDLASIARLRIAKGVNDNF did not. CHO S745 cell attachment to MKKTRG-contg. peptides was partially decreased. A 36% decrease in CHO K1 cell attachment to the N-terminus was also obsd. when the heparin-binding consensus sequence KKTR was mutated to QNTR. In addn., peptide MKKTRG partially inhibited (25% inhibition) CHO K1 cell attachment to the N-terminus. However, peptide MKKTRG was not sufficient to fully promote cell attachment to the N-terminus of TSP-1. Peptides VDAVRTEKGFLLLASLRQ and TLLALERKDHS also supported CHO K1 cell attachment in a GAG-dependent and -independent manner, resp. Moreover, CHO K1 cell attachment to MKKTRG was found to be markedly enhanced when flanked with the sequences VDAVRTEKGFLLLASLRQ and TLLALERKDHS. Peptide VDAVRTEKGFLLLASLRQMKKTRG nearly abolished (98% inhibition) CHO K1 cell attachment to the N-terminus, while peptides MKKTRG, MKKTRGTLLALERKDHS, and VDAVRTEKGFLLLASLRQ had only a moderate inhibitory effect (25, 27, and 53% inhibition, resp.). These data indicate that the sequence VDAVRTEKGFLLLASLRQMKKTRGTLLALERKDHS (residues 60-94) constitutes a GAG-dependent cell adhesive site in the N-terminus of TSP-1. Moreover, a GAG-independent site, encompassing residues 189-200 (FQGVLQNVRFVF), has been identified. These two adhesive sites supported the attachment of a wide variety of cells (human breast **carcinoma**, melanoma, and osteosarcoma cells), and a high degree of sequence homol. was found between TSP-1 and **TSP-2** between residues 60 and 94 (48% identity) and 189-200 (67% identity), further suggesting the functional importance of these two cell adhesive sites in the N-terminus

of TSP-1.

L28 ANSWER 31 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:720738 HCAPLUS
DOCUMENT NUMBER: 126:17266
TITLE: Regression of thrombospondin-1 expression, a natural inhibitor of angiogenesis, in polyoma middle T transformed NIH3T3 cells
AUTHOR(S): Sheibani, Nader; Frazier, William A.
CORPORATE SOURCE: Dep. Biochemistry Molecular Biophysics, Washington Univ. Sch. Med., St. Louis, MO, 63110, USA
SOURCE: Cancer Lett. (Shannon, Irel.) (1996), 107(1), 45-52
CODEN: CALEDQ;.ISSN: 0304-3835
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Thrombospondi-1 (TS1) is a modular extracellular matrix glycoprotein and expressed by many cell types in culture. Thrombospondin-1 inhibits angiogenesis and its expression inversely correlates with the degree of invasiveness and metastasis in **tumor** cell lines. Here, we demonstrate that expression of Polyoma middle T oncogene in NIH3T3 cells results not only in transformation but also represses expression of three thrombospondin isoforms, TS1, TS2, and TS3. Similar results were obsd. in ras, and to a lesser extent in src transformed NIH3T3 cells. Middle T and ras transformed cells expressed higher levels of c-jun mRNA, while the src transformed cells expressed higher levels of junB mRNA when compared to control cells. Thus, repression of thrombospondin levels appears to play an important role in establishment and maintenance of a **malignant** phenotype. This is mediated, at least in part, by alteration in c-jun activity in middle T and ras transformed NIH3T3 cells.

L28 ANSWER 32 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:380455 HCAPLUS
DOCUMENT NUMBER: 125:77961
TITLE: Isolation of genes differentially expressed in human primary myoblasts and embryonal rhabdomyosarcoma
AUTHOR(S): Genini, Michele; Schwalbe, Petra; Scholl, Florence A.; Schafer, Beat W.
CORPORATE SOURCE: Department Pediatrics, University Zurich, Zurich, CH-8091, Switz.
SOURCE: Int. J. Cancer (1996), 66(4), 571-577
CODEN: IJCNAW; ISSN: 0020-7136
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Using a subtractive hybridization method, we have cloned 48 cDNAs which are expressed in human primary myoblasts but down-regulated in the embryonal-rhabdomyosarcoma (RMS) cell line RD. Twenty-nine sequences could be identified as coding for previously known gene products, while I9 encode unknown proteins. Twelve clones coding for known proteins that were highly down-regulated in the RD cells were chosen for further anal. on Northern blots contg. addnl. normal and RMS cells. The expression pattern of TGF-.beta.-induced gene product-3 (.beta.igH3), inhibitory G-protein alpha subunit (G.alpha.2), osteoblast-specific factor-2 (OSF-2), 22-kDa smooth-muscle protein (SM22), clone A335I (homologous to mouse talin), testican, thrombospondin-I and **thrombospondin-2** suggests involvement of these proteins in the genesis of the **neoplastic** phenotype. Among the clones with unknown sequence, several are identical or homologous to expressed sequence tags or known cDNAs, such as integrins or laminin. These results suggest that several isolated clones might have an important role in the detn. or maintenance of the normal phenotype, and thus their loss is possibly involved in the progression of **malignancy**.

L28 ANSWER 33 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:270844 HCAPLUS
DOCUMENT NUMBER: 124:309241

TITLE: The cDNA sequence, chromosomal location and characterization of two novel cDNAs in humans: **thrombospondin 2** and **dermal** fibroblast heparan sulfate n-deacetylase/n-sulfotransferase
AUTHOR(S): Labell, Terry Lee
CORPORATE SOURCE: Univ. of Washington, Seattle, WA, USA
SOURCE: (1996) 98 pp. Avail.: Univ. Microfilms Int., Order No. DA9609695
From: Diss. Abstr. Int., B 1996, 56(12), 6559
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable

L28 ANSWER 34 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:693972 HCAPLUS
DOCUMENT NUMBER: 121:293972
TITLE: Properties of recombinant mouse **thrombospondin 2** expressed in Spodoptera cells
AUTHOR(S): Chen, Hui; Sottile, Jane; O'Rourke, Karen M.; Dixit, Vishva M.; Mosher, Deane F.
CORPORATE SOURCE: Dep. Med. Biomol. Chem., Univ. Wisconsin, Madison, WI, 53706, USA
SOURCE: J. Biol. Chem. (1994), 269(51), 32226-32
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A baculovirus system was used to express full-length recombinant mouse **thrombospondin 2** (rTSP2) as a disulfide-bonded homotrimer with an N-terminus beginning with Asp20. RTSP2, like TSP1, was more sensitive to trypsin digestion if depleted of Ca2+. The trypsin digestion pattern of rTSP2 and TSP1 differed in that trypsin cut between the first and second type 1 modules of rTSP2. For bovine aortic endothelial cells adhering to TSP-coated polystyrene plates, redn. after coating caused both TSPs to be much more adhesive; these adhesions were blocked completely by RGDS peptide or antibody to .alpha.v.beta.3 integrin. RTSP2 and TSP1 also mediated the adhesion of HT-29 human colon **adenocarcinoma** cells that carry .alpha.v.beta.5 but not .alpha.v.beta.3 integrin. Antibody to .alpha.v.beta.5 did not inhibit adhesion of HT-29 cells to TSP1 or rTSP2. Rather, adhesion of HT-29 cells was decreased by treatment of TSPs with EDTA, abolished by redn. of the TSPs, and, in the case of rTSP2, blocked by heparin. Adhesion of MG63 cells to both TSPs was complex. Treatment with EDTA enhanced the adhesive activity of rTSP2 but decreased the adhesive activity of TSP1. These results show that TSP2 can be processed and secreted when overexpressed using baculovirus, TSP1 and rTSP2 differ in protease susceptibility in the type 1 module region, and TSP1 and rTSP2 mediate cell adhesion by complex and similar but not identical mechanisms.

L28 ANSWER 35 OF 35 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:103007 HCAPLUS
DOCUMENT NUMBER: 120:103007
TITLE: Differential expression of thrombospondin 1, 2, and 3 during murine development
AUTHOR(S): Iruela-Arispe, M. Luisa; Liska, DeAnn J.; Sage, E. Helene; Bornstein, Paul
CORPORATE SOURCE: Dep. Biol. Struct., Univ. Washington, Seattle, WA, 98195, USA
SOURCE: Dev. Dyn. (1993), 197(1), 40-56
CODEN: DEDYEI; ISSN: 1058-8388
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Thrombospondin 1 is a secreted, trimeric glycoprotein that mediates interactions between cells and extracellular matrix and exhibits cell-specific effects on migration and proliferation. Recently, two addnl. thrombospondin genes (**thrombospondin 2** and 3)

have been identified. To study the functions of these proteins, the authors have used in situ hybridization and RNase protection assays to compare the expression of the genes encoding thrombospondin 1, 2, and 3 during murine embryogenesis. Thrombospondin mRNAs were assocd. with ossification, neuronal organogenesis, and lung development, although transcripts were differentially expressed. Thrombospondin 1 was predominant from days 10 to 13. During this period, high but transient levels of expression were obsd. in the neural tube, head mesenchyme, and cardiac cushions. In contrast, a more const. level of thrombospondin 1 mRNA was apparent in resident megakaryocytes of the liver, as well as in circulating megakaryocytes; neither **thrombospondin 2** nor 3 was detected in these cells. Thrombospondin 1 was also produced by cells of the developing kidney and gut. The expression of **thrombospondin 2** was confined principally to organized connective tissue that included pericardium, pleura, perichondrium, periosteum, meninges, ligaments, and reticular **dermis**. **Thrombospondin 2** was also produced by differentiating skeletal myoblasts and by cells of the kidney and gut. Moreover, high levels of expression were detected in blood vessels. Thrombospondin 3 mRNA was restricted to brain, cartilage, and lung. Although thrombospondin 1, 2, and 3 belong to a family of structurally related genes, the differences obsd. in the spatiotemporal distribution of the corresponding mRNAs indicate unique functions for these secreted proteins.

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=> d stat que l31

L21           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "THROMBOSPONDIN 2 (CATTLE
                CLONE P268C1 PRECURSOR)"/CN
L22           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "THROMBOSPONDIN-2 (HUMAN
                CLONE PSECTAG)"/CN
L23             SEL  PLU=ON  L21 1- CHEM :        3 TERMS
L24             SEL  PLU=ON  L22 1- CHEM :        3 TERMS
L25           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L23
L26           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L24
L27          88 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L25 OR L26 OR (THROMBOSPONDIN?
                 OR TSP)(W)2
L28          35 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L27 AND (?CANCER? OR ?CARCINOM
                ? OR ?TUMOR? OR ?NEOPLAS? OR ?MALIG? OR SKIN OR ?DERM?)
L30           6 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (THROMBOSPONDIN(W)II) AND
                (?CANCER? OR ?CARCINOM? OR ?TUMOR? OR ?NEOPLAS? OR ?MALIG? OR
                SKIN OR ?DERM?)
L31           5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L30 NOT L28


=>

=>

=> d ibib abs hitrn l31 1-5


L31  ANSWER 1 OF 5  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         1997:477785  HCAPLUS
DOCUMENT NUMBER:          127:188943
TITLE:                    Human ornithine decarboxylase-overproducing NIH3T3
                          cells induce rapidly growing, highly vascularized
                          tumors in nude mice
AUTHOR(S):                Auvinen, Merja; Laine, Aire; Paasinen-Sohns, Aino;
                          Kangas, Anneli; Kangas, Lauri; Saksela, Olli;
                          Andersson, Leif C.; Holtta, Erkki
CORPORATE SOURCE:         Department of Pathology, Haartman Institute,
                          University of Helsinki, Helsinki, FIN-00014, Finland
SOURCE:                   Cancer Res. (1997), 57(14), 3016-3025
                          CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER:                American Association for Cancer Research
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DOCUMENT TYPE: Journal
LANGUAGE: English
AB Overexpression of human ornithine decarboxylase (ODC) under the control of strong promoters induces morphol. transformation of immortalized NIH3T3 and Rat-1 fibroblasts. We demonstrate here that ODC-overproducing NIH3T3 cells are **tumorigenic** in nude mice, giving rise to rapidly growing, large fibrosarcomas at the site of inoculation. The **tumors** are capable of invading host fat and muscle tissues and are vascularized abundantly. To disclose the mol. mechanism(s) driving the **tumorigenic**, invasive, and angiogenic phenotype of the **tumors**, the ODC-overproducing cell lines and **tumor** tissues were analyzed for the expression of various potential regulators and mediators of cell proliferation, matrix degrdn., and angiogenesis. The **tumorigenicity** of ODC transformants was assocd. with elevated polyamine levels and down-regulated growth factor receptors. The invasiveness of the ODC-induced **tumors** could not be attributed to overexpression of various known extracellular matrix-degrading proteases or matrix metalloproteinases. The induction of the **tumor** neovascularization proved not to be elicited by vascular endothelial growth factor or basic fibroblast growth factor. Instead, the ODC-over-expressing cells appeared to secrete a novel angiogenic factor(s) that was able to promote migration of bovine capillary endothelial cells in collagen gels and increase the proliferation of human endothelial cells in vitro. In parallel, ODC-transformed cells displayed down-regulation of thrombospondin-1 and -2, the neg. regulators of angiogenesis. Thus, the induction of the angiogenic phenotype of the ODC transformants is likely due both to increased expression and secretion of the new angiogenesis-stimulating factor(s) and decreased prodn. and release of the antiangiogenic thrombospondins.

L31 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:105685 HCAPLUS
DOCUMENT NUMBER: 126:210379
TITLE: Thrombospondin-1 and -2 messenger RNA expression in normal, benign, and **neoplastic** human breast tissues: correlation with prognostic factors, **tumor** angiogenesis, and fibroblastic desmoplasia
AUTHOR(S): Bertin, Nicolas; Clezardin, Philippe; Kubiak, Robert; Frappart, Lucien
CORPORATE SOURCE: Dep. of Pathology and CNRS UMR 5641 and INSERM Research Unit 403, Edouard Herriot Hospital, Lyon, 69437, Fr.
SOURCE: Cancer Res. (1997), 57(3), 396-399
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Thrombospondin-1 (TSP1) is a Mr 450,000 extracellular matrix glycoprotein that modulates **tumor** growth, angiogenesis, and metastasis. Of the five structurally different TSPs described to date, only TSP2 is similar to TSP1 in terms of its mol. architecture, and TSP2 also modulates angiogenesis. Angiogenesis plays a relevant role in the biol. aggressiveness of breast **cancer**, and TSP1 is present in the **tumor** stroma (termed desmoplasia) of invasive human breast ductal **carcinoma** not otherwise specified (NOS). The present study was designed to identify and quantify TSP1 and TSP2 mRNAs in normal, benign, and **neoplastic** human breast tissues using the reverse transcriptase PCR technique. The authors found that TSP2, like TSP1, was expressed in human breast tissues, and that TSP1 and TSP2 mRNA expression in invasive breast **carcinoma** NOS was significantly increased compared to that obsd. in normal and benign tissues. The expression of TSP1 and TSP2 in invasive breast ductal **carcinoma** NOS did not significantly correlate with any of the prognostic factors studied (**tumor** size, lymph node status, morphol., and hormone receptor status). However, when the authors' study population was divided

according to the quantity of **tumor** stroma, TSP1 (and possibly TSP2) mRNA expression and microvessel counts in desmoplastic-rich stroma of breast **carcinoma** NOS were significantly increased compared to those obsd. in desmoplastic-poor stromata.

L31 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:213772 HCAPLUS
DOCUMENT NUMBER: 120:213772
TITLE: Modulation of thrombospondin expression during differentiation of embryonal **carcinoma** cells
AUTHOR(S): Liska, Deann J.; Hawkins, Richard; Wikstrom, Kristina; Bornstein, Paul
CORPORATE SOURCE: Dep. Biochem., Univ. Washington, Seattle, WA, 98195, USA
SOURCE: J. Cell. Physiol. (1994), 158(3), 495-505
CODEN: JCLLAX; ISSN: 0021-9541
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The thrombospondins (TSPs) are a family of extracellular glycoproteins that display distinct patterns of temporal and spatial expression during development. In this study, the authors investigated the expression of two of the TSPs-TPS1 and TSP2-during the course of differentiation of embryonal **carcinoma** cells in vitro. The authors report that both TSP1 and TSP2 mRNA and protein synthesis are induced during the differentiation of P19EC cells into neutrons, glial cells, and fibroblasts. Immunofluorescence studies indicate that TSP1 displays a fibrillar pattern of staining, characteristic of an extracellular matrix protein, in differentiated P19EC cells. In contrast, TSP2 is cell-assocd. and is present on differentiated P19EC cells and on primary neurons and glial cells obtained from a 17-day embryonic mouse cerebral cortex. Interestingly, although both TSP1 and TSP2 are more prevalent in areas of differentiated cells, they display distinct patterns of deposition. These observations suggest that TSP1 and TSP2 may function differently during neurogenesis. The response of TSP1 and TSP2 to differentiation of P19EC cells indicates that this cell system will serve as a valuable model for the study ot TSP expression and function during neurogenesis.

L31 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:641374 HCAPLUS
DOCUMENT NUMBER: 119:241374
TITLE: Method and composition for inhibiting angiogenesis
INVENTOR(S): Bouck, Noel P.; Polverini, Peter J.; Good, Deborah J.; Frazier, William A.
PATENT ASSIGNEE(S): Northwestern University, USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9316716	A1	19930902	WO 1993-US1652	19930222

W: CA, JP
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
PRIORITY APPLN. INFO.: US 1992-841656 19920224
AB Peptides derived from human thrombospondin are useful for inhibiting angiogenesis and thereby preventing the growth of **tumors**. Thus, Ser-Pro-Trp-Ser-Ser-Ala-Ser-Val-Thr-Ala-Gly-Asp-Gly-Val-Ile-Thr-Arg-Ile-Arg inhibited FGF-induced migration of bovine capillary endothelial cells in vitro (ED50 0.6 .mu.M), and pellets contg. this peptide and basic FGF implanted in the rat cornea inhibited angiogenesis.

L31 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:34622 HCAPLUS

DOCUMENT NUMBER: 118:34622
TITLE: **Thrombospondin II**: partial cDNA sequence, chromosome location, and expression of a second member of the thrombospondin gene family in humans
AUTHOR(S): LaBell, Terry L.; Milewicz, Dianna J. McGookey; Disteche, Christine M.; Byers, Peter H.
CORPORATE SOURCE: Dep. Pathol., Univ. Washington, Seattle, WA, 98195, USA
SOURCE: Genomics (1992), 12(3), 421-9
CODEN: GNMCEP; ISSN: 0888-7543
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A novel form of human thrombospondin was identified during the screening of a human fibroblast cDNA library. The cDNA sequence for **thrombospondin II** is reported for 1.8 kilobases (kb) of the 3'-end of the cDNA, plus an addnl. 937 base pairs of 3'-untranslated sequence. The translated sequence revealed a high degree of similarity to thrombospondin I. The homol. ranged from 56 to 80% for different regions within the 2 proteins. The repeating segments of amino acid sequence identified in thrombospondin I were conserved in **thrombospondin II**. The new form of thrombospondin hybridized to a 7.5-kb message by Northern anal. The THBS2 gene, which codes for **thrombospondin II**, was located at the distal long arm of chromosome 6 at 6q27. The gene was transcribed in fibroblasts, smooth muscle cells, and an osteosarcoma cell line, at levels somewhat lower than that of thrombospondin I. Umbilical vein endothelial cells did not transcribe **thrombospondin II** under the conditions of this study. These findings suggest that previous studies of thrombospondin function need to be reassessed to identify the functions specific to each mol.